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Case Report Section

A new case of adult Acute Myeloid Leukemia with t(3;3)(p24;q26)

Bo Yuan, Janice Smith, April Ewton, Sai Ravi Pingali, Arthur Zieske, Amy Breman

Department of Molecular & Human Genetics, Baylor College of Medicine (BY, JS, AB), Houston, TX 77030, USA. Baylor Genetics (BY, JS, AB), Houston, TX 77030, USA, by2@bcm.edu; breman@bcm.edu. Department of Pathology Genomic Medicine, Houston Methodist Hospital (AE, AZ), Houston, TX 77030, USA. Department of Medicine, Houston Methodist Hospital (SRP), Houston, TX 77030, USA.

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Abstract

Case report on a new case of adult Acute Myeloid Leukemia with t(3;3)(p24;q26).

Clinics

Age and sex
68 years old female patient.

Previous history
No preleukemia; no previous malignancy; no inborn condition of note

Organomegaly
No hepatomegaly; splenomegaly (acute splenomegaly); no enlarged lymph nodes; no central nervous system involvement

Blood

WBC: 9.13; RBC: 2.37X 10^9/l
HB: 6.7g/dl
Platelets: 11X 10^9/l
Blasts: 5%

Cyto-Pathology Classification

Phenotype
AML with a translocation or inversion in chromosome 3; Refractory acute myelogenous leukemia with poor risk cytogenetics, pancytopenia secondary to refractory AML, acute Splenomegaly, fatigue, petechiae, dyspnea on exertion, neutropenic fever, refractory thrombocytopenia with hematuria and persistence of disease.

Immunophenotype
CD34: positive in blasts that account for 45% of cellularity; CD61: positive in megakaryocytes. MPO: Positive in background myeloid cells. Negative in blasts. E-Cadherin and glycophorin: Highlights markedly decreased erythroid precursors

Rearranged Ig Tcr Not performed

Pathology
The marrow cellularity is approximately 90% (biopsy/clot); Erythroid elements: Markedly decreased number. Normoblastic; Myeloid elements: Left shifted with increased blasts. Blasts account for 18% of cells in the dilute aspirate and about 45 of cells in the CD34 immunostained biopsy. Eosinophilia is seen on biopsy specimen; Megakaryocytes: Markedly increased in number with clustering and markedly dyspoietic morphology (small hypolobulated, dysjointed nuclei, hyperlobed); Reticulin stain shows Grade 1 fibrosis.

Electron microscopy Not performed

Diagnosis
Acute myelogenous leukemia

Survival

Date of diagnosis 02-2017

Treatment

Reduced dose of anthracycline therapy due to cardiac function; Cytarabine and idarubicin; Dacogen; Nivolumab; Decitabine; Hydroxyurea
Complete remission: no
Treatment related death: no
Relapse: no

Status Alive

Last follow up 05-2017

Survival 3 months

Karyotype

Sample Bone marrow

Culture time 24 and 48 hours unstimulated cultures

Banding GTG banding

Results
45,XX,t(3;3)(p24;q26),-7[20]

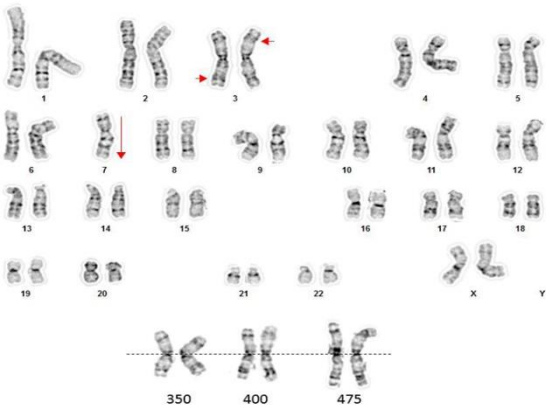

Figure 1. Karyotype of the cell line demonstrating the t(3;3)(p24;q26) and loss of a copy of chromosome 7 (red arrows). The lower panel shows the abnormal chromosomes 3 at increasing band resolution.

Other molecular cytogenetics technics
Fluorescence in situ Hybridization (FISH)

Other molecular cytogenetics results
Confirmatory FISH using the Cytocell EVI1 Breakapart Probe (REF: LPH 036-A / LPH 036-A50) was performed on cells harvested from 24 hour bone marrow culture. The FISH probe mixture consists of a 156 kb probe telomeric to the D3S4415 marker including the LRRC34 gene (red, R), a 179 kb probe including the entire EVI1 (MECOM) gene plus flanking regions (green, G), and a 559 kb probe centromeric to the EVI1 gene including the D3S3364 marker (aqua, A), all within the 3q26.2 region. Interphase cells showed a 1R/1GA/1RGA signal pattern, corresponding to one split red/green signal with the aqua signal remaining with the green signal, confirming the translocation breakpoint between the EVI1 and LRRC34 genes (Figure 2). However, the partner of EVI1 resulting from the translocation remains unknown.

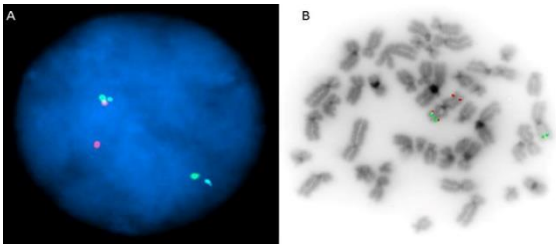

Figure 2. FISH using the Cytocell EVI1 Breakapart Probe demonstrating the breakpoint at 3q26.2 between EVI1 and LRRC34, a gene telomeric to EVI1, in both interphase (A) and metaphase cells (B).

Comments

Rearrangements involving the 3q26 region have been described in up to 10% of acute myeloid leukemias (AML), chronic myeloid leukemias in blast crisis (CML BC), and myelodysplastic syndrome (Poppe 2006). The most common rearrangement is a paracentric inversion of the long arm, inv(3)(q21q26), although multiple rearrangements of this region have been described (Huret 2005, Jancuskova 2014, Lawce 2017). While the breakpoints are variable and may include translocations, inversions or other structural complexities, they unanimously result in EVI1 overexpression. Interphase FISH assays have been used to detect rearrangements involving the EVI1 locus at 3q26 (Wieser 2003). Monosomy 7 is also frequently present, and is associated with a poorer prognosis (Haferlach 2012, Huret 2005, Lugthart 2010). While multiple partners have been identified for EVI1, the partner of EVI1 in rearrangements involving 3p24 and 3q26 is unknown. Similar to the current case, a pericentric inversion involving both the short and long arms of chromosome 3, inv(3)(p24q26), has been reported in ten cases (Haferlach 2012), with elevated EVI1 expression reported. Therefore, identification of the partner gene warrants further investigation.

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